Everything you ever wanted to know about MyPeBS
QUESTIONS & ANSWERS

MyPeBS
Personalising
Breast Screening

Dear Madam,

In this booklet you will find answers to many of the questions you may have regarding your participation in MyPeBS. If you would like further clarification, please do not hesitate to contact the study doctors / investigators or health professionals involved in the study.

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An explanation of some of the technical terms used in this booklet (marked with an "*") is provided in the Glossary section at the end.

europa.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 755394

QUESTIONS ANSWERED BY THIS GUIDE

THE PROJECT

1. WHAT DOES MyPeBS STAND FOR?

"My Personal Breast cancer Screening"

2. WHAT IS THE AIM OF MyPeBS?

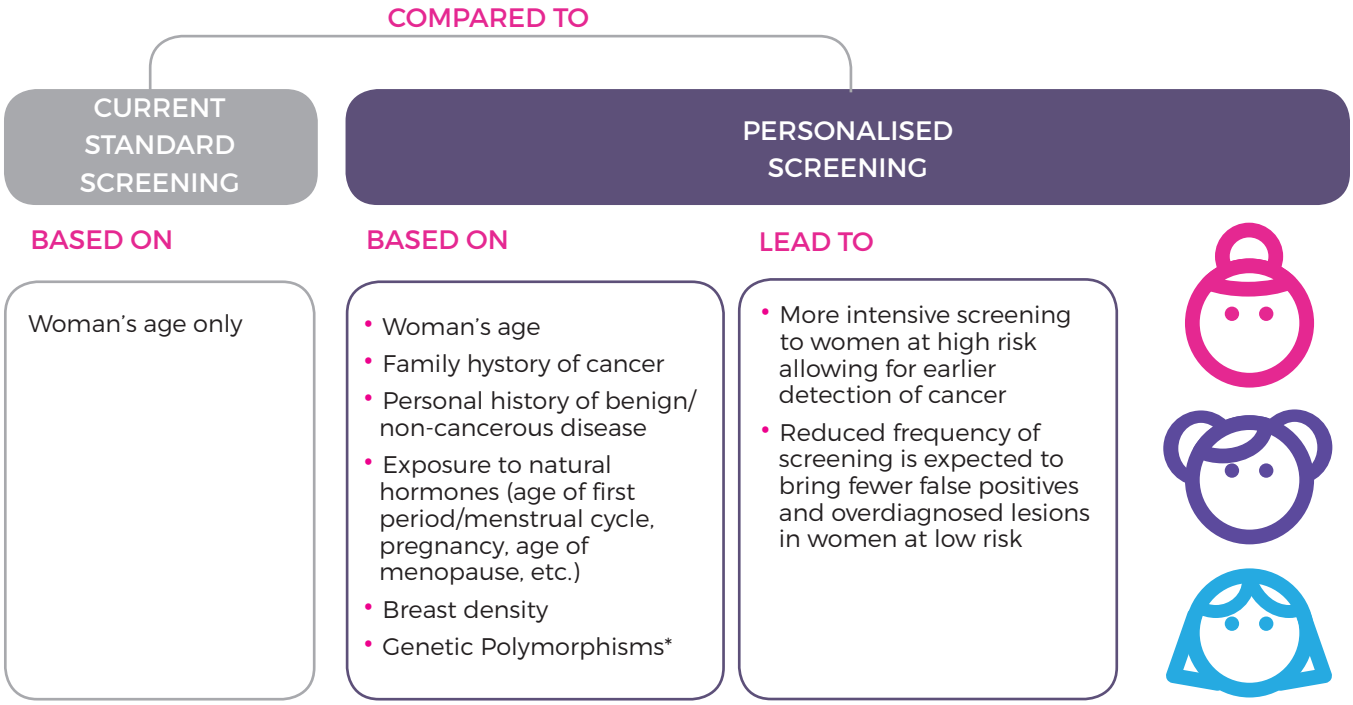
MyPeBS aims at evaluating the effectiveness of more personalised breast cancer screening compared to current standard practices.

The main goal is to assess if breast cancer screening adapted to a woman's projected 5-years risk of breast cancer is **at least as** effective as current standard screening in women aged 40 to 70-years old for the prevention of advanced breast cancer. We will also test if it is **more** effective than current standard (reduction of advanced cancers).

MyPeBS will also assess whether this personalised risk-adapted screening strategy will reduce negative potential consequences of standard screening: unnecessary biopsies related to false positive findings*, overdiagnosis*, or overtreatment* particularly in women at low risk. In addition, we will compare the socio-psychological impact and socioeconomic characteristics of the two screening strategies, assessing women's satisfaction, anxiety, etc. Finally, we will assess in each country (Belgium, France, Israel, Italy, and the United Kingdom), if the results obtained with these screening strategies justify the resources used.

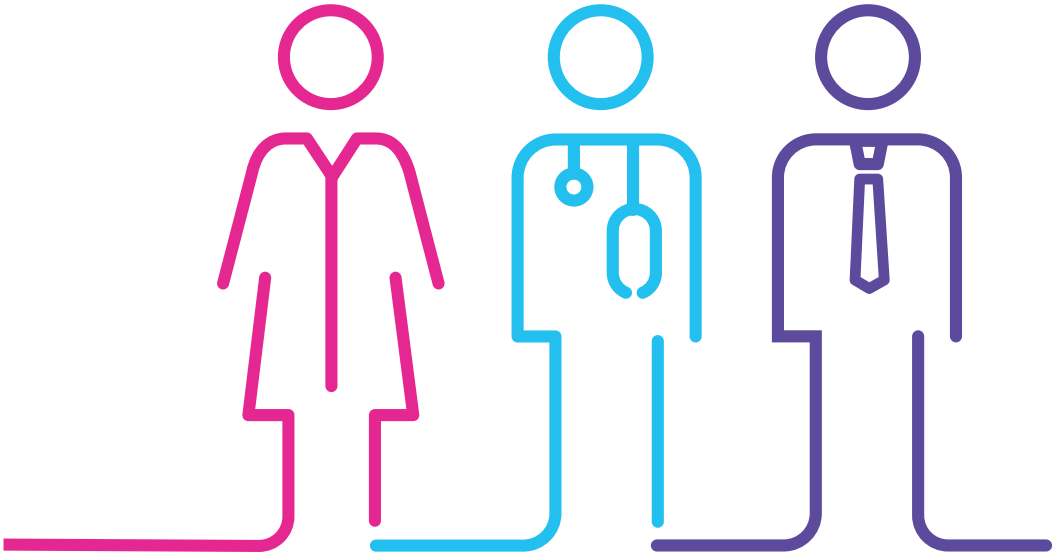
After analysing all the results of the study, MyPeBS will propose general recommendations for more effective breast cancer screening in Europe.

BOX 1. MyPeBS MAIN GOAL.



3. WHO COORDINATES MyPeBS?

MyPeBS was designed and is coordinated by an international group of doctors, researchers, and scientists, all experts in breast cancer prevention and screening, together with patient advocates.
The study sponsor is UNICANCER, a non-profit federation of French hospitals dedicated to oncology, a European academic sponsor of clinical research in oncology. In participating countries, there are several trial sites coordinated by the national principal investigator.



4. WHO FUNDS MyPeBS?

MyPeBS is mainly funded by the European Union. This project has received funding from the European Commission's Horizon 2020 research and innovation programme under grant agreement No 755394. MyPeBS is also cofounded by its partners.

5. WHICH COUNTRIES PARTICIPATE IN MyPeBS?

Belgium, France, Israel, Italy, and the United Kingdom.

6. WHICH SCREENING PROGRAMMES PARTICIPATE IN MyPeBS?

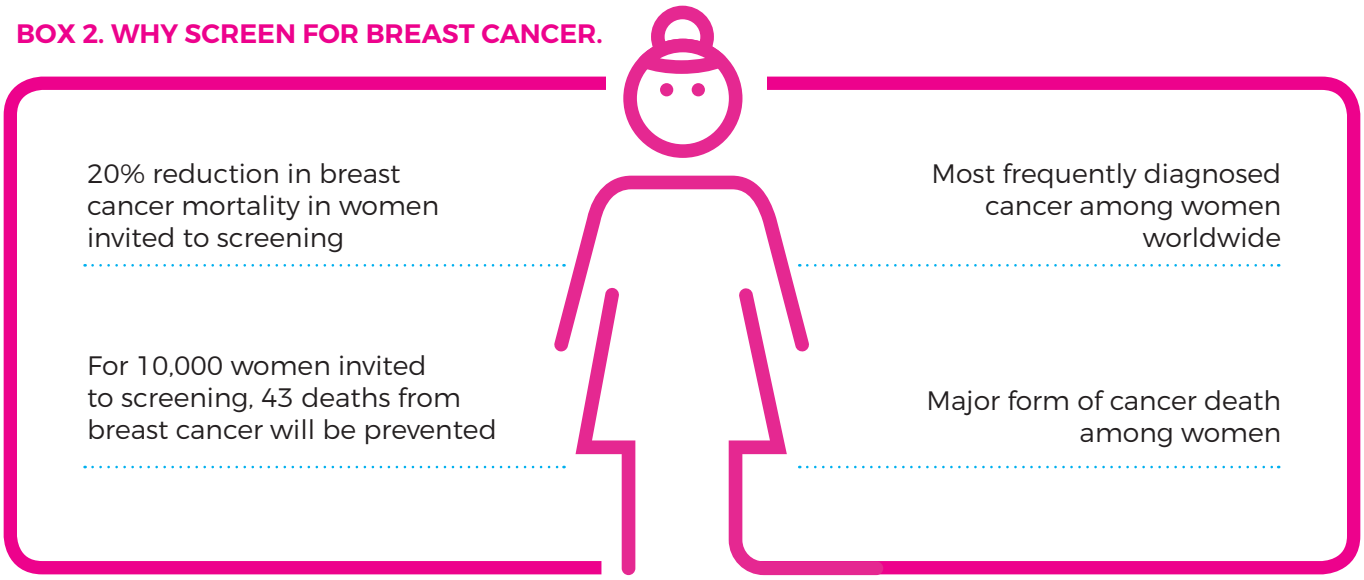
The countries and regions which are expected to recruit women in the MyPeBS study are the following:
Belgium: Brussels, Vlaanderen (Leuven), and Walloon.
France: National-basis (30 departments are participating).
Israel: Maccabi Healthcare Services (HMO) members performing studies at Assuta Medical Centers.
Italy: Florence, Lombardy, Reggio Emilia, Romagna, Turin, Veneto.
United Kingdom: Cambridge, Leeds, Manchester.

WHAT DO WE KNOW ABOUT BREAST CANCER SCREENING AND WHY DO WE NEED THE MyPeBS STUDY?

7. WHY SCREEN FOR BREAST CANCER?

Breast cancer is the most common cancer in Western women. It is a serious disease as approximately **one in five women** diagnosed with breast cancer unfortunately die from it. **Appropriate cancer screening enables early detection of cancer**, the treatment of which is generally less intense and with greater chances of recovery compared with cancers diagnosed at a more advanced stage. **Screening is therefore a major cornerstone of the fight against breast cancer**.

BOX 2. WHY SCREEN FOR BREAST CANCER.



Sources: Stewart BW, Wild CP and International Agency for Research of Cancer (2014). World Cancer Report 2014. Lyon: IARC Press. Independent UK Panel on Breast Cancer Screening (2012). The benefits and harms of breast cancer screening: an independent review. Lancet. 2012 Nov 17;380(9855):1778-86.

8. HOW IS BREAST CANCER SCREENING IMPLEMENTED IN PARTICIPATING COUNTRIES?

In Western countries, breast cancer screening consists of regular mammograms* (radiological examinations of both breasts with two images per breast). This is part of national organised screening systems which include monitoring of screening quality and, in most countries, double reading of the mammograms by certified radiologists and radiographers.

Apart from women already identified with very high specific risk factors (e.g. germline mutation of BCRA1/2, PALB2, TP53 or equivalent significant family history), **age is the only criterion for starting organised screening**. Depending on the country, mammograms are offered every 1 to 3 years, starting from the age of 45 years until between 69-74 years.

Currently in Belgium	• All women aged 50-69 are invited every 2 years to have a mammogram. • Women with known very high specific risk factors (such as significant family history, germline mutations, personal breast or ovarian cancer history, chest radiotherapy history) are eligible for reimbursed screening at a younger age, with higher frequency of testing, including MRI.
Currently in France	• Organized breast cancer screening concerns women aged 50-74, who are invited to have a mammogram* every two years. • Only a few women, with very high specific risk factors have more intensive screening: women with a predisposing genetic modification, or those who had chest radiotherapy before the age of 25, or who already had breast cancer or a precancerous lesion.
Currently in Israel	• All women aged 50-74 are invited every 2 years to have a mammogram. • Women with higher specific risk factors (such as significant family history, germline mutations, and others) may start screening at a younger age, have higher frequency of testing and, in very high risk women, have additional testing.
Currently in Italy	• Women aged 50-69 are invited every two years to have a mammogram. • Some regions invite women aged 45-49 (annual mammography) and 70-74 (biennial mammography). • Only a few women, those identified with very high specific risk factors follow a different screening pathway.
Currently in UK	• Women aged 50-70 are invited every three years to have a mammogram. Only a few women, with very high specific risk factors have more intensive screening (predisposing genetic modification, those who had chest radiotherapy before the age of 25, those who have already had breast cancer or a precancerous lesion).

9. WHAT ARE THE BENEFITS OF MAMMOGRAPHIC SCREENING?

Breast cancer screening usually involves regular mammograms*.

Apart from women already known to be at very high risk of developing breast cancer, age is the only criterion for starting screening. Depending on the country, mammograms are offered every 1 to 3 years, starting from the age of 45-50 years until 69-74 years.

These screening recommendations are based on large-scale studies that have shown that screening reduces breast cancer deaths by about 20%, i.e. preventing one in five deaths.

Mammographic screening, also reduces the number of stage 2 and higher cancers at diagnosis in women older than 50.

Earlier detection of cancer, at a less advanced stage, reduces breast cancer deaths and allows for less intense treatment.

Of note, **national organised screening programmes integrate monitoring of screening quality and double reading (when possible) of the mammograms by certified radiologists and radiographers.** Double reading increases the cancer detection sensibility. Certified radiologists and radiographers are responsible for quality of the diagnostic performance.

BOX 3. BENEFITS OF MAMMOGRAPHIC SCREENING

10. WHAT ARE THE LIMITS AND DISADVANTAGES OF BREAST CANCER MAMMOGRAPHIC SCREENING?

Current screening by mammography does have some limits and disadvantages:

Insufficient efficacy:

· Mammography does not detect all cancers and some (around 15%) may appear during the time between two invitations or screening mammograms. These are called interval cancers* and are considered a failure of the screening.

· A significant proportion of cancers are still diagnosed at an already advanced stage (around 25-30%).

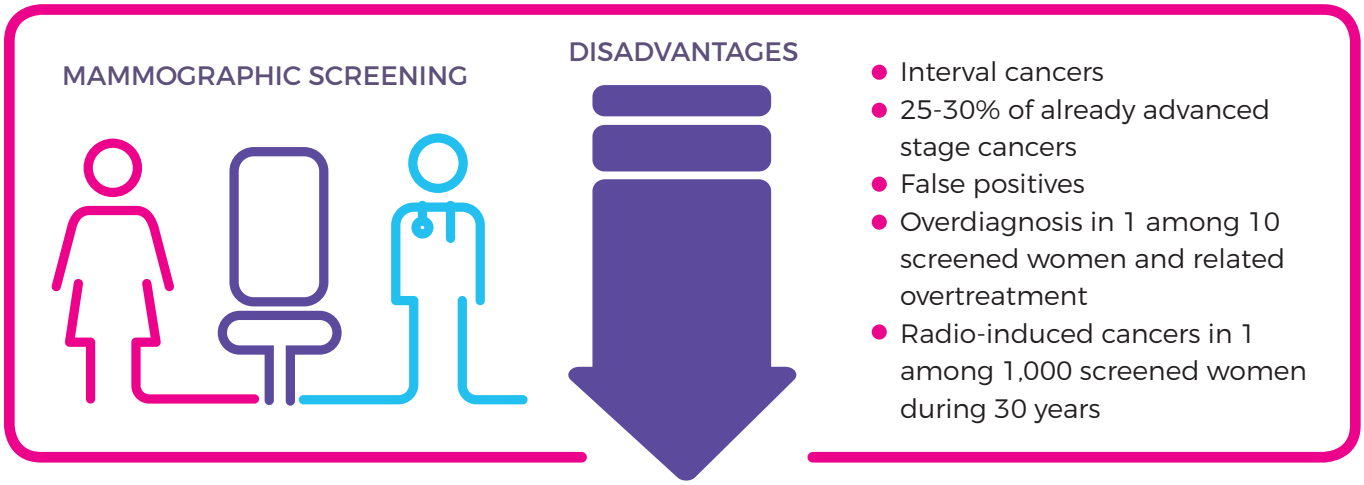
Unintended "adverse effects":

· False positives*: A small percentage of screening mammograms leads to additional recalls for further investigation or biopsies* for what turns to be a benign/non-cancerous lesion.

· Overdiagnosis*, leading to overtreatment*: A number of cancers which are diagnosed (estimated on average about 10% i.e. 1 in 10) by breast screenings are growing so slowly that they would never cause problems during the woman's life, leading to unnecessary biopsies and treatment.

· Radio-induced cancers*: Mammography delivers a small dose of X-rays which in the long-term can increase the risk of breast cancer. However, this risk is extremely low (about 1 in 1,000 women screened during 30 years) compared to the benefits of early diagnosis. Radiation doses delivered in screening are very closely monitored.

BOX 4. LIMITS AND DISADVANTAGES OF MAMMOGRAPHIC SCREENING.



11. HOW CAN WE ESTIMATE INDIVIDUAL BREAST CANCER RISK FOR POTENTIALLY MORE EFFECTIVE "TARGETED" SCREENING?

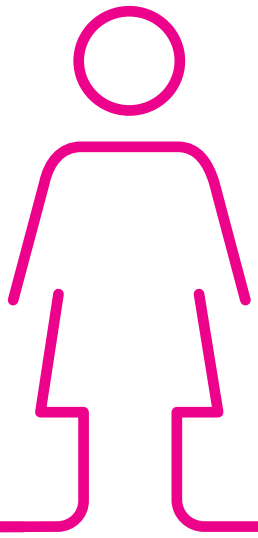
Our ability to identify women at higher or lower risk of developing breast cancer should make targeted breast cancer screening possible. This would result in **offering more intensive screening for women at higher risk and reduced screening for those at lower risk.** Reduced screening may lower the risk of the unintended adverse effects of breast cancer screening: false positives, overdiagnoses, and over-treatments. E.g. useless biopsies of benign lesions.

To do this, we need to estimate the individual risk of breast cancer in each woman in the general population.

Over the last twenty years, European and American research teams have developed **risk "scores",** to estimate a woman's risk of developing breast cancer. These scores are now well-established and widely validated, especially in Europe. They use simple personal and clinical data like the **woman's age, family history of cancer, personal history of benign/non-cancerous disease, and exposure to natural hormones** (age of first period/menstrual cycle, pregnancy, age of menopause etc.), and medical hormones (hormone replacement treatments, the contraceptive pill etc.). As part of every mammogram performed, the **breast density** is assessed in each woman and this "breast density score" also contributes to predicting individual risk.

In the last ten years, European and American researchers have been able to show that **genetic polymorphisms*** (variations in the sequence of certain genes, in a substantial portion of the population) influence the individual risk of developing breast cancer. At present, more than 300 of these polymorphisms have been described. Each individual variation only contributes a small amount of risk. However, a score that includes about a hundred polymorphisms becomes much more predictive. **Finally, by combining conventional clinical risk scores (created using data as described above) with the influence of polymorphisms we can identify women with different levels of breast cancer risk with more certainty.**

BOX 5. ELEMENTS CONSIDERED FOR CALCULATING BREAST CANCER PERSONAL RISK-SCORES.



PERSONALISED RISK-BASED SCREENING

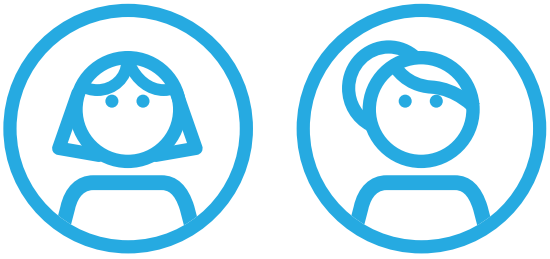
Personal risk scores are based on:

- Woman's age
- Family history of cancer
- Personal history of benign/non-cancerous disease and exposure to natural hormones (age of first period/menstrual cycle, pregnancy, age of menopause etc.)
- Medical hormones (hormone replacements treatments, the contraceptive pill etc.)
- Breast density score
- Genetic polymorphisms

Personalised screening based on evaluating each woman's risk of developing breast cancer with a score using both clinical data (described above) and polymorphisms is now feasible, and should be more effective. It will allow us to offer more intensive screening in women at high risk (i.e. more frequent mammography + additional radiological exams if needed), possibly with earlier detection of cancer which is associated with more favourable outcome and less intensive treatments. In women at low risk, a reduced frequency of screening is expected to lower the risk of the unintended adverse effects of breast cancer screening: false positives, overdiagnoses, and overtreatments.

BOX 6. POTENTIAL BENEFITS OF PERSONALISED BREAST CANCER SCREENING.

WOMEN AT HIGH RISK



More intensive screening, possibly with earlier detection of cancer which is associated with more favourable outcome and less intensive treatments.

WOMEN AT LOW RISK

Reduced frequency of screening, expected to lower unintended adverse effects of breast cancer screening (false positives, overdiagnoses, overtreatments).

MyPeBS aims to test this hypothesis. In MyPeBS, **two groups of women will be compared:** a group of women who will follow standard breast screening and a group of women who will follow a screening programme adapted to their individual estimated breast cancer risk. This "risk-based screening" will include a mammogram, performed at various intervals depending on the woman's risk, and for women with much higher than average risk, a Magnetic Resonance Imaging (MRI*) examination, plus a breast density evaluation by ultra-sound in case of dense breast tissue detected during the mammography.

PARTICIPATING IN MyPeBS

12. WHAT ARE THE CRITERIA FOR PARTICIPATING IN MyPeBS?

Women from the general population will be eligible for the study if they fulfil the following criteria. These will be checked with the study doctor/investigator during the enrolment:

- Women (whether born female or not) aged 40 to 70 years old (inclusive)
- Women living in participating regions and programmes from countries involved in MyPeBS: Belgium, France, Israel, Italy, United Kingdom
- The most recent mammography must be normal (in a woman who has had one)
- Willingness and ability to comply with scheduled visits, and other trial procedures (for information on trial procedures see question 16)
- Sufficient understanding of any of the languages used in the study
- Women affiliated with a social security/ national healthcare system
- Written informed consent obtained
- (Only for women in Israel): Women belonging to Maccabi Healthcare Services (HMO) performing their studies at Assuta Medical Centers.

13. UNDER WHICH CIRCUMSTANCES WOULD A WOMAN NOT BE ABLE TO PARTICIPATE IN MyPeBS (EXCLUSION CRITERIA)?

In the following cases, women will not be able to participate in MyPeBS:

- Personal history of breast cancer, either invasive or ductal carcinoma in situ
- Prior history of atypical breast lesion, lobular carcinoma in situ or chest wall irradiation
- Knowledge or suspicion of very high predisposing condition to breast cancer: germline mutation of BCRA1/2, PALB2, TP53 or equivalent
- History of bilateral mastectomy
- Recent abnormal breast finding under work-up (clinically suspect lesion or BI-RAD 4 or 5 image)
- Inability to provide signed informed consent
- Insufficient understanding of any of the available languages
- Psychiatric or other disorders that are not compatible with compliance to the protocol requirements and follow-up
- Women who will not be able or do not intend to be followed-up for 4 years
- Women for whom it is impossible to have access to internet during the study

14. HOW MANY WOMEN ARE EXPECTED TO PARTICIPATE IN MyPeBS?

The study will include 85,000 women. The target number of women by country is: 10,000 in Belgium, 20,000 in France, 15,000 in Israel, 30,000 women in Italy, and 10,000 in the United Kingdom.

15. HOW LONG DOES PARTICIPATION LAST IN MYPEBS?

Each woman will be asked to participate in the study for 4 years from her date of entry into the study.

16. WHAT WOULD MY PARTICIPATION IN MyPeBS CONSIST OF?

Women living in one of the regions in countries participating in MyPeBS, and considered to be eligible to participate (for eligibility criteria see question 13), are invited to join the study.

While graph 1 summarizes the pathway you will follow if you agree to participate in MyPeBS, Tables 1 to 3 explains each step in detail.

FIGURE 1. SIMPLIFIED SCHEME OF THE PATHWAY TO BE FOLLOWED BY WOMEN PARTICIPATING IN MyPeBS.

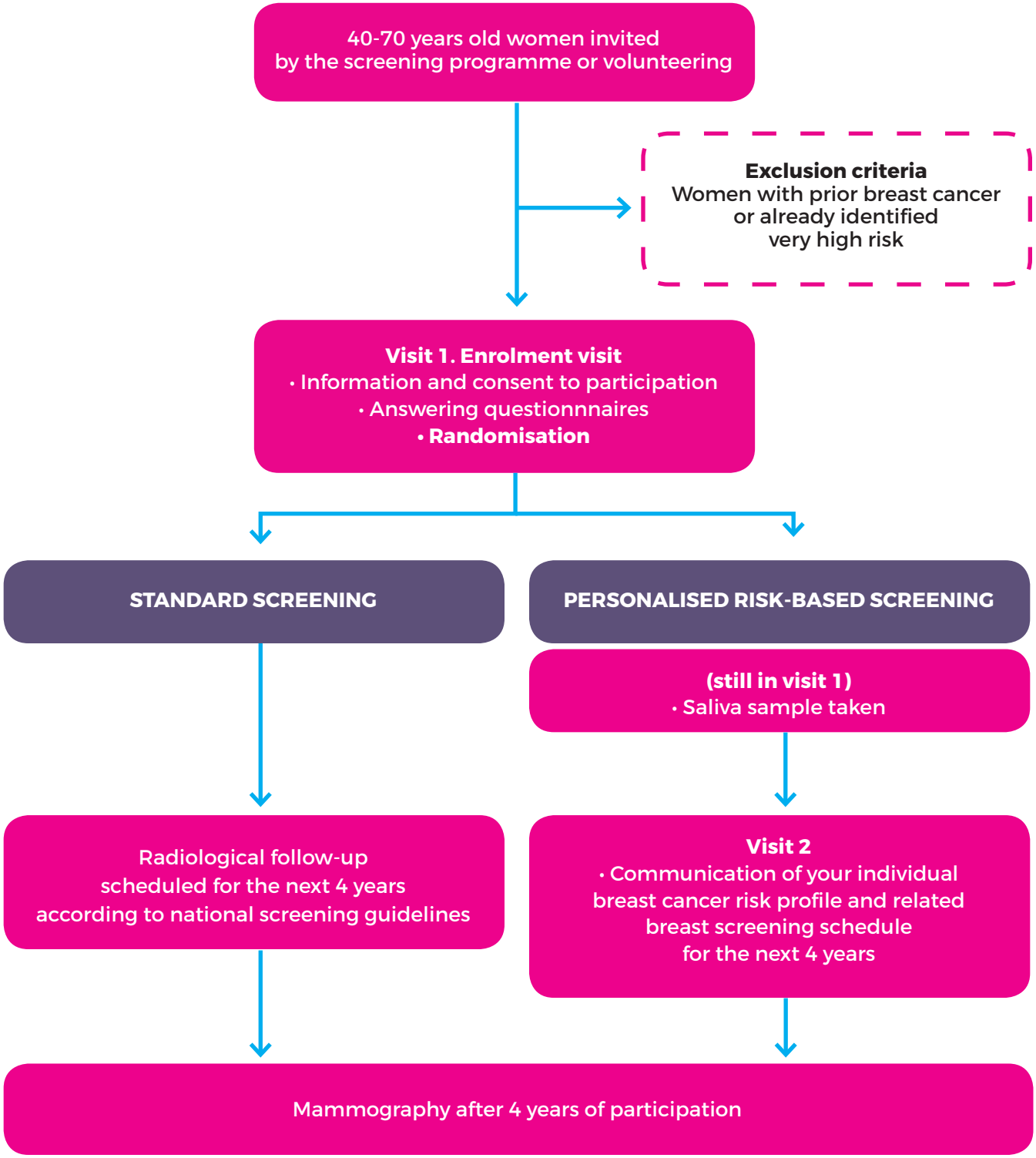
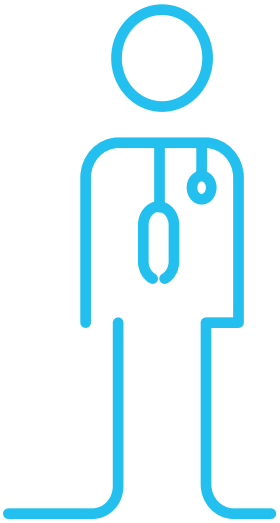


TABLE 1. DETAILED DESCRIPTION OF THE PATHWAY TO BE FOLLOWED BY WOMEN PARTICIPATING IN MyPeBS DURING VISIT 1.

VISIT 1. ENROLMENT VISIT



1. INFORMATION AND CONSENT TO PARTICIPATION

The study investigator (doctor or other health professional – *depends on national protocols*) will explain MyPeBS to you, and provide you with a detailed information sheet and an informed consent form. If you decide to participate in the study, you will need to sign this document.

The visit could be done in two parts, if you wish to take a reflection period before signing the informed consent form this will be possible. In this case, you will be able to call the screening programme to ask for an appointment to complete this visit.

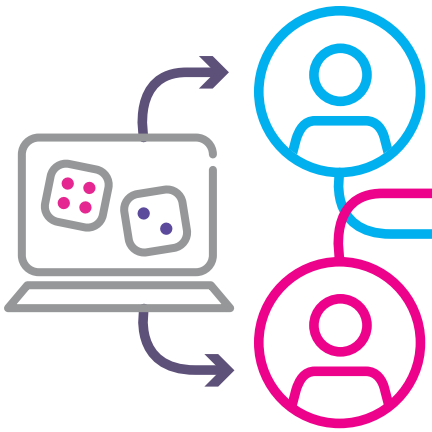
Once you sign the informed consent you will receive a unique identification number that will be used throughout the study.

2. ANSWERING QUESTIONNAIRES

You will be asked to answer **two questionnaires** (online). This will take around 30 minutes of your time, it can be done at the health professional's office (waiting room/mammography centre).

Questionnaires:

1. About your personal and family medical history, and lifestyle
2. Your level of anxiety, and your understanding of the information received.



3. RANDOMISATION

MyPeBS is a randomised study, which means that you will be randomly assigned (by a computer) to one of two screening programmes:

GROUP 1: STANDARD SCREENING

or

GROUP 2: PERSONALISED RISK-BASED SCREENING

Thus, women will have a 1 in 2 (50%) chance of being in either program.

The randomisation will be done immediately by your investigator upon your signature of the informed consent, and you will immediately have the result.

What happens after the randomisation?

You will be immediately informed of the result of the randomisation. Then, according to the group you are allocated to, the next steps will be organised:

TABLE 2. DETAILED DESCRIPTION OF WHAT HAPPENS WHEN YOU ARE RANDOMISED.

STANDARD SCREENING GROUP	PERSONALISED RISK-BASED SCREENING
Breast screening schedule delivery If you are randomised into **Group 1**, you will receive immediately your breast screening schedule for the next four years (the duration of your study participation) following the current standard procedures of your respective country.	**Saliva sampling** If you are randomised into **Group 2**, you will be asked to provide a saliva sample. This sample will be used to analyse your DNA to search for genetic polymorphisms* that will help estimate your personal risk of developing breast cancer in the next 5 years. You will not receive your breast screening follow-up schedule yet. Upon receipt of your risk estimation results including DNA results, you will have a **second visit**, about 10-12 weeks after visit 1.

TABLE 3. RISK ANNOUNCEMENT VISIT (VISIT 2).

PERSONALISED RISK-BASED SCREENING

1. Communication of your individual breast cancer risk profile

If you are randomised into the "personalised risk-based screening" group your **individual breast cancer risk profile** will be given and explained to you through a face-to-face or telephone visit by the study doctor / investigator around 10 to 12 weeks after the initial visit.

Your breast cancer risk estimation will also be communicated to you by a written result sheet that can be printed by the doctor/investigator during the visit and that you will be able to download from your personal MyPeBS portal.

2. Delivery of your personalised breast screening schedule

At the same visit, you will receive your breast screening schedule for the next four years (the duration of your study participation) tailored to your breast cancer risk profile.

All women participating (both women randomised in the standard screening group, and women randomised in the personalised risk-based screening group) will have a personal portal online for MyPeBS study in which you will be able to:

- Follow all information on the trial over the next 4 years
- Receive reminders of scheduled screening appointments
- Fill-in yearly questionnaires for which you will receive notices and reminders
- Inform researchers of any relevant events/changes that may impact your participation in the study (examples: moving, breast cancer in your family)
- (Only for women in the personalised risk-based screening group) Find risk recalculation if needed based on reported events you have reported (such as new personal and family history of cancer).

For additional information on the MyPeBS personal portal, see questions 41 to 45.

17. WHICH QUESTIONNAIRES SHOULD I COMPLETE DURING MY PARTICIPATION IN MYPEBS?

Regardless of the screening program to which you are allocated, at the **first visit** the study doctor/ investigator will ask you to complete two online questionnaires:

(1) A questionnaire about your personal and family medical history, and lifestyle
(2) A questionnaire describing your level of anxiety, risk of cancer perception and your understanding of the information received

We will also ask you some general questions to be able to describe the characteristics of women participating in MyPeBS.
All study data will be de-identified*, so that it will be impossible to identify you outside of your personal secured space in the participants' portal of the study. Your name, surname and contact details will only be known by those responsible for your clinical care but they will not be revealed to researchers or others.

After 3 months, 1 year, and 4 years from the first visit we will kindly ask you to complete the questionnaires on psychological follow-up and satisfaction. These questionnaires are available online in your private study portal.

Completion of these questionnaires should not take more than 30 minutes. It is very important you give us your feedback through these questionnaires, we thank you in advance for that!

18. CAN I CHOOSE WHETHER I PARTICIPATE IN THE STANDARD SCREENING GROUP OR IN THE PERSONALISED RISK-BASED SCREENING GROUP?

No, you can't. MyPeBS is a randomised study, which means that women who wish to participate will be randomly allocated (by a computer) to one of the two screening programs: standard screening or risk-based screening. Thus, women will have a 1 in 2 (50%) chance of either standard screening, according to their age and country, or personalised screening according to their estimated individual breast cancer risk.

It is not possible to choose the allocated group, since the validity of the study is based on the fact that the allocation is random and includes no biases. This is the sole way to be objective in the interpretation of the results.

19. HOW IS A WOMAN'S BREAST CANCER RISK PROFILE CALCULATED (ONLY FOR WOMEN ALLOCATED TO THE "PERSONALISED RISK-BASED SCREENING" GROUP?)

If you are **randomised into the "personalised risk-based screening**" group, your individual risk of developing breast cancer within 5 years will be calculated based on:

- Your **personal and family history** (taken from the questionnaire you will be asked to complete during visit 1)
- Your **breast density** (obtained through the screening test)
- A **DNA analysis of your saliva** (sample obtained at visit 1).

20. IF I AM RANDOMISED TO THE STANDARD SCREENING GROUP CAN I STILL BE INFORMED ABOUT MY PERSONAL RISK?

If you are in the **standard screening group**, we will not be able to provide you with the same evaluation of breast cancer risk as in the other group. Indeed this requires a saliva sample, DNA analyses and use of computerised algorithms that will not be available outside of the other group.
Indeed this is not yet a standard.

However, you can discuss your general risk factors, and also how to decrease breast cancer risk with your doctor/health professional. You can receive such general information and personal information from your investigator upon request.

21. HOW DOES THE ANALYSIS OF GENETIC POLYMORPHISMS IN THE SALIVA DNA HELP ESTIMATE BREAST CANCER RISK?

In this research, if you are **randomised to the "personalised risk-based screening" group**, you will be asked to have a saliva test at the first visit. This test requires you to provide some saliva. Sampling takes a few minutes at most. This will be done during your inclusion visit.

Your sample will be identified by a bar code on the tube neither your name nor surname nor any other means of identification will be used.

The sample will be analysed by the study's centralised platform. **This analysis should take 10-12 weeks.**

The testing method uses a standardised "DNA chip" with a large number of genetic polymorphisms* (between 600,000 and 900,000). Around 300 polymorphisms known and validated for predicting breast cancer risk will be used to estimate your individual risk of breast cancer. One DNA variation alone does not confer a significant high or low risk, however the use of the combination of 300 variations is much more predictive. **The result of the tests on these 300 polymorphisms will be used together with your clinical and radiological data to estimate your risk of developing breast cancer within 5 years.**

Your individual risk level will be communicated to you by your doctor/investigator* and then made available on your private online space on the MyPeBS web platform.

The complete polymorphism tests results (between 600,000 and 900,000) will be stored confidentially and may be used during the study to re-estimate your risk. For instance, if new polymorphisms, are identified during the study your risk score will be re-estimated using the saliva test results from the first visit. If this occurs, or if there is a change in your risk score, you will be informed. However, the chance of a significant change in your risk score is extremely low. These test results may also be used for additional research in the future, but will not be communicated to you as part of MyPeBS.

No other routine genetic analysis will be carried out for this study (except for Israeli women who will also be tested for BRCA1/2 Ashkenazi mutations). However, if you are considered as having a hereditary predisposition given your family history, you will be advised to attend an oncogenetic consultation. Your study doctor/investigator can provide you with more information, if you need.

22. ARE ANY ADDITIONAL GENETIC ANALYSES CARRIED OUT FOR SPECIFIC GROUPS OF WOMEN?

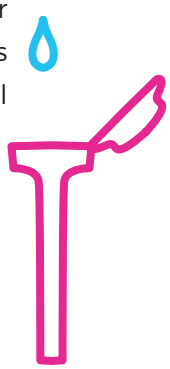
Yes there are. For **participants in Israel** the results of single nucleotide polymorphisms* will be linked to Ashkenazi founder mutation-linked polymorphisms (BRCA1 and BRCA2) for risk calculation. An additional specific informed consent is included in Israel.

- The results of these SNPs will be only provided to women accrued in Israel after adequate information.
- The results of these SNPs will either indicate: YES, a founder mutation is probably present or NO, no such mutation is likely.
- The results of these SNPs will not have any medico-legal value and will only indicate the need for a dedicated genetic counselling if positive. This will be followed by genetic testing including clinical DNA sequencing towards identification of such germline mutations, if eventually present. The women will be classified at very high risk until they have a confirmed result based on sequencing.
- Negative results will not have a medico-legal value. This technique is not a substitute for a full clinical consultation and testing according to medical guidelines, and may have a sensitivity a little lower than 100%.

23. WHAT HAPPENS WITH RESIDUES THAT REMAIN AFTER THE SALIVA TEST?

If you are randomised into the "**personalised risk-based screening"** and if you consent to donate the DNA residue that will remain after the saliva test, it will be stored in a fully secure, de-identified DNA bank, specifically opened for the MyPeBS study. This residue may be used for future research, such as more complete sequencing of all genes.

This residue will only be used for ethically approved research purposes and neither you nor your doctor will receive these results.



24. WHAT BREAST CANCER RISK CATEGORIES HAVE BEEN DEFINED IN MyPeBS (PERSONALISED RISK-BASED SCREENING GROUP)?

In MyPeBS study, only women assigned to the **"personalised risk-based screening"** group will be given their estimated breast cancer risk .
Your estimated risk of developing an invasive* cancer will be expressed verbally as a risk category (low, average, high, or very high). If you prefer, the risk level can be given as a percentage, so that you can compare your personal risk to that of women of a similar age.
Breast cancer risk levels are shown in table 4.

TABLE 4 – BREAST CANCER RISK CATEGORIES

	LOW RISK	AVERAGE RISK	HIGH RISK	VERY HIGH RISK
Estimated risk of invasive breast cancer projected at 5 years	 risk <1%	 1% ≤ risk < 1.67%	 1.67% ≤ risk < 6%	 risk ≥ 6%
Meaning of the percentage	A woman with a **low risk** has a less than 1% chance (1 in 100 women) of developing invasive breast cancer within the next 5 years (this is lower than the average risk for a 45-year-old woman in Europe).	A woman with a **average risk** has between 1 and 1.67% chance of developing invasive breast cancer within 5 years (1 in 60 women).	A woman with a **high risk** has between 1.67 and 6% chance of developing invasive breast cancer within 5 years (1 in 30 women).	A woman with a **very high risk** has more than 6% chance of developing invasive breast cancer within 5 years (1 in 16 women).

25. WHAT IS THE CORRESPONDING SCREENING SCHEDULE FOR EACH RISK CATEGORY?

In MyPeBS, only women assigned to **"personalised risk-based screening"** will be given their estimated breast cancer risk and given a screening schedule for the next four years. Women with an average, high, or very high risk profile might have additional radiological examinations if required: ultrasound and/or magnetic resonance. A mammogram (and magnetic resonance in specific cases) might also be required at study entry if a recent one is not already available.
Table 5 illustrates the screening schedule (tests and intervals) for each risk category.

TABLE 5 – SCREENING SCHEDULE FOR EACH RISK CATEGORY.

	LOW RISK	AVERAGE RISK	HIGH RISK	VERY HIGH RISK
Mammogram*	After 4 years	Every 2 years	Every year	Every year
Additional examination	-	Ultrasound if high breast density	Ultrasound if high breast density	MRI every year until age 60

Mammogram can be replaced by digital breast tomosynthesis* (3D mammogram) according to local rules.

The radiologists and radiographers involved in the standard breast screening will perform mammograms for risk-based screening using procedures identical to those used for the standard screening (examination quality, second reading, etc.) Only the schedule will vary.

You will receive your examination results and a detailed written report of your mammogram or digital breast tomosynthesis* exactly as you would have had for standard breast screening.

Regardless of your screening programme and schedule, a mammogram is required after 4 years of participation, at the end of the study. The date and result must be entered on the web platform. The end-of-study mammogram will be indicated on your screening schedule.

26. HOW CAN I BE SURE THAT I REMEMBER MY NEXT EXAMINATION?

Close to the date of your scheduled examination(s) you will receive a reminder by email.

You can also check your schedule at any time in your personal space on the web platform.

27. CAN MY RISK PROFILE CHANGE DURING THE LIFESPAN OF THE PROJECT?

If you have been randomised into the **"personalised risk-based screening"**, your risk profile may change during the lifespan of the project based on two different circumstances: (1) change in your personal characteristics or family history; (2) evolution of the knowledge on genetic polymorphisms*.

- **Personal and family history:** A significant event (such as you having a breast biopsy or someone in your family being diagnosed with a breast cancer) may change your risk profile. If this happens, a new screening schedule will be delivered to you. So, having updated information on your personal and family history is crucial for us in order to reassess your screening schedule if needed; this is the reason why we kindly ask you to update your personal data on the study's web platform during your entire study participation (at least each year for 4 years).
- **Genetic polymorphisms* test:** The saliva sample you have given during visit 1 will be analysed, and based on the result of the polymorphisms analysis, your estimated risk of developing breast cancer within 5 years will be estimated. The complete polymorphism test results will be stored confidentially and may be used during the study to re-estimate your risk. For instance, if new polymorphisms of major interest are identified by scientists during the study, your risk score could be re-calculated. If this occurs and if there is a change in your risk profile, you will be immediately informed. However, the chance that this happens is extremely low.

28. WHAT SHOULD I EXPECT FROM MAMMOGRAMS PERFORMED DURING THE STUDY?

Mammograms of women assigned to both groups, whether "standard screening" or "personalised risk-based screening", will be performed by radiologists and radiographers involved in the standard breast screening programme. Depending on national guidelines, in both groups radiologists may use either standard mammography or a new technique called digital breast tomosynthesis* (DBT). This new technology produces 3D and reconstructed (synthetic) radiological images of the breast. It has been approved by European Guidelines as an alternative to standard mammography.

You will receive your examination results and a detailed written report of your mammogram or digital breast tomosynthesis* exactly as you would have for standard breast screening.

Mammograms (and ultrasound) results will be scored according to the current standard and Bi-RAD classification:

- BI-RAD ACR 1: normal breasts.
- BI-RAD ACR2: normal breast, presence of typically benign images.
- Bi-RAD ACR3: presence of an image that needs to be reexamined after a few months to make sure it is absolutely benign.
- BI-RAD ACR4: presence of an image that requires a biopsy.
- Bi-RAD ACR5: presence of a very suspect image that requires biopsy.

29. WHAT HAPPENS IF I DON'T FOLLOW MY SCREENING EXAMINATION SCHEDULE?

We would be grateful if you could follow your screening examination schedule, as closely as possible, regardless of the screening programme allocated. This is important for you but also for MyPeBS in order to obtain accurate results.

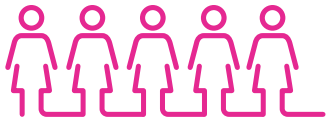
However, if for any reason you can't follow the schedule, please inform your study doctor / investigator and report the reason why in your personal space on the MyPeBS web platform.

30. WHAT ARE THE EXPECTED BENEFITS RELATED TO PARTICIPATION IN THIS STUDY?

Table 6 illustrates the expected benefits related to participation in the study.

TABLE 6 – EXPECTED BENEFITS FOR PARTICIPATION IN THE STUDY.

Women allocated to standard breast screening



No specific benefit is expected except more information and awareness about breast cancer risk, breast screening and prevention, which we will update during the study. Data obtained from study participants, including your data, may change the future of breast cancer screening in Europe. Once we publish the results of MyPeBS, and if personalised risk-based screening becomes the standard, you may be offered risk-based screening in the future.

Women allocated to the personalised risk-based screening

Women with high/very high risk: examinations are planned more frequently than standard screening. In this case, if unfortunately you develop breast cancer, it may be detected at an earlier stage than in standard conditions.

- We estimate that out of all women assigned to risk-based screening (42,500), about 50 women will be diagnosed with breast cancer at an earlier stage than via the standard screening, preventing about 50 stage 2 and higher cancers*.
- A diagnosis at an earlier stage is associated with a better prognosis and less intense treatments.
- We also hope to see fewer cancers develop between two negative screening visits (interval cancers*) in this group.

Women with low level risk: Fewer examinations are planned than with standard screening. This may:

- Reduce the risk of false positive findings*.
- Reduce the risk of overdiagnosis* and associated overtreatments (surgery/anticancer treatment).
- Reduce stress/anxiety induced by these unnecessary examinations.
- Reduce the very low risk of cancers* due to X-ray exposure.

31. WHAT ARE THE POTENTIAL RISKS AND SIDE EFFECTS RELATED TO PARTICIPATION IN THIS STUDY?

Table 7 illustrates the potential risks and side effects related to participation in the study.

TABLE 7 – POTENTIAL RISKS AND SIDE EFFECTS OF PARTICIPATION IN THE STUDY.

Women allocated to standard breast screening

There are no expected additional risks or side effects (for the advantages and disadvantages of standard screening see question 9 and 10).

Women allocated to the personalised risk-based screening

- **Women with low level risk** (who will have fewer mammograms than with standard screening): small risk of a cancer being detected later than with standard screening (estimated risk of 1 woman per 1,000).
- **Women with high/very high risk** (who will have more frequent mammograms than with standard screening): there could be more false positives than with standard screening, as well as more overdiagnoses and overtreatments, which may cause unnecessary anxiety. Increased exposure to X-rays may lead to a very low risk of radio-induced malignancies.

For women in both groups

The medical risks of radiological examinations (mammograms, ultrasound and MRIs) undertaken during the study are identical to risk of these examinations done routinely.

32. WHO SHOULD I CONTACT IN THE EVENT OF MEDICAL QUESTIONS OR PROBLEMS DURING THE STUDY?

Please contact your community practice physician (referring doctor) for any health problems.

If you have specific questions or issues regarding the study, you can contact your study doctor or health professional who included you into the trial.

33. WILL I BE PAID FOR PARTICIPATING IN THE STUDY?

No, you won't be paid for participating in the study.

34. DO I HAVE TO PAY FOR EXAMINATIONS DONE WITHIN THE STUDY?

You will not have to pay for the screening mammograms nor the ultrasounds or screening MRI examinations, if you are having these, or any other procedure scheduled within the study.

35. WHAT HAPPENS IF THE RESULTS OF THE EXAMINATIONS CARRIED OUT DURING THE STUDY ARE NOT NORMAL?

If an abnormal finding is confirmed and further investigation is required (a repeat mammogram or ultrasound, additional MRI examination, biopsy or treatment), all the arrangements will be organised according to standard practice by your radiologist and/or referring doctor*.

If investigations of this type are necessary, we would appreciate if you could complete the relevant section in your personal space on the web platform. Reporting this information is very important and your cooperation is essential.

If you have a confirmed breast cancer, you will receive care and treatment according to the applicable national rules and according to good practice guidelines. Your referring doctor will be in charge of organising your health care. If this occurs, we would be grateful if you could report it using your personal space on the web platform. In addition, we would be grateful if you would indicate the treatment(s) proposed.

36. WHAT SHOULD I DO IF I NOTICE AN ABNORMALITY IN MY BREAST(S)?

Regardless of your allocated screening schedule, if you notice an abnormality in your breasts (deformation, nipple discharge, lumps etc.) you should consult your referring doctor* as soon as possible. Your referring doctor will organise complementary tests/examinations, if necessary.

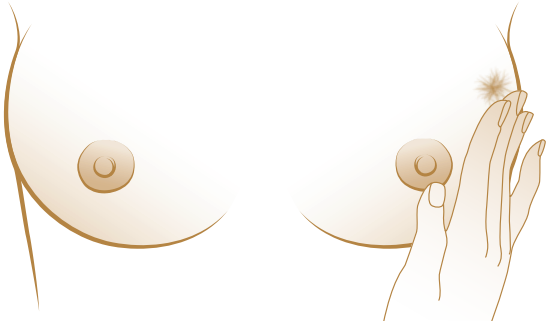
Remember that even if your breast cancer risk was estimated to be low, breast cancer may still occur. Low risk is not no risk.

Also, a negative screening (normal mammogram) test does not mean that there is no risk at all in the next coming years, and it is better to remain aware of your body signals.

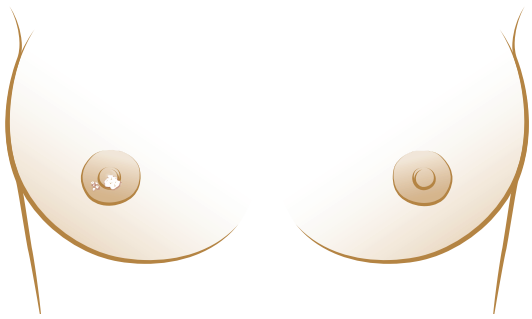
It is good that you know your breasts so that you may notice any change.

TABLE 8 ILLUSTRATES POTENTIAL ABNORMAL FINDINGS THAT COULD LEAD YOU TO SEE YOUR REFERRING PHYSICIAN.

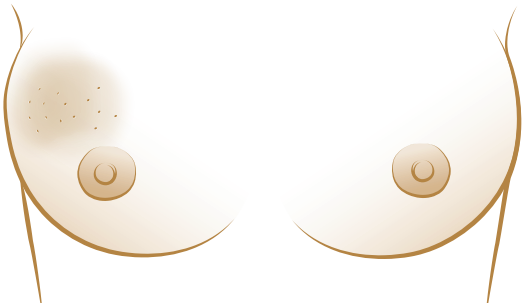
Lump, hard knot or thickening inside the breast or underarm area



Itchy, scaly sore or rash on the nipple

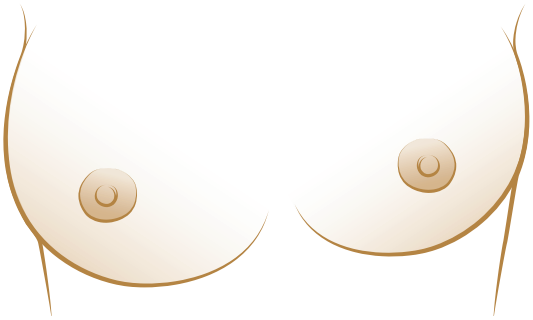


Swelling, warmth, redness or darkening of any part of the breast



Pulling in of your nipple or other parts of the breast

Change in the size or shape of the breast



Nipple discharge that starts suddenly

Dimpling or puckering of the skin

New pain in one spot that doesn't go away

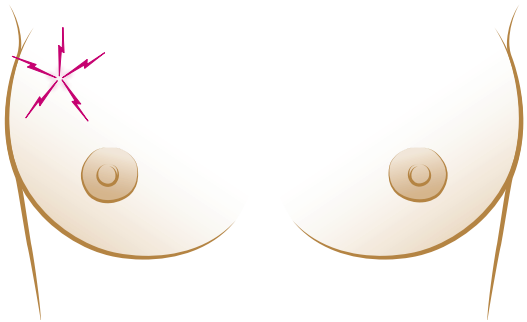


Illustration by Susan G. Komen ®

37. ARE MAMMOGRAPHY IMAGES STORED DURING THE STUDY AND FOR WHAT PURPOSE?

The pseudonymised (absence of name, birth date, or any data with which you could be identified) images obtrained from mammographic exams performed during the study will be, wherever possible, stored for potential further research. If you consent for your images to be stored, they may be transmitted to a central database dedicated in MyPeBS or stored locally.

These images would be available for research projects either within MyPeBS or other studies, related to screening, assessing breast density and risk prediction. They may be used to develop or test diagnostic and screening tools in the future.

38. CAN I LOWER MY RISK OF BREAST CANCER?

Even though there is no way to totally prevent breast cancer, some risk factors can be changed lowering your risk.

Table 9 illustrates **some recommendations made to all women** that could help lowering your risk.

TABLE 9 – SOME RECOMMENDATIONS MADE TO ALL WOMEN ARE:

KEEP A HEALTHY BODY WEIGHT

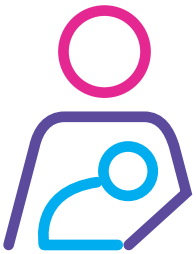
Both increased body weight and weight gain as an adult are linked with a higher risk of breast cancer after menopause, especially of advanced breast cancer. It is recommended to stay at a healthy weight throughout your life and avoid excess weight gain by balancing your food intake with physical activity.

BE PHYSICALLY ACTIVE IN EVERYDAY LIFE. LIMIT THE TIME YOU SPEND SITTING.

Being physically active reduces the likelihood of breast cancer.
There are a number of biological mechanisms through which physical activity might protect against cancer. These include effects of physical activity on blood sugar levels and insulin and related hormones, sex hormones, inflammation, and immune function, all of which affect cancer risk. Physical activity also helps keep you from gaining weight and helps in maintaining a healthy body weight – which will have an additional effect on reducing cancer risk. Do as much light activity as possible (such as standing, walking, light bicycling, stretching, climbing the stairs, doing housework, and participating in leisurely sports such as table tennis or golf). In addition, important health benefits can be expected when trying to engage in at least 150 minutes of physical activity of moderate intensity per week, or 75 minutes of physical activity of vigorous intensity per week, or an equivalent combination of moderate- and vigorous-intensity activity, if possible. Examples of moderate-to-vigorous physical activities are weight-bearing endurance, resistance types of physical activity (i.e. exercise training), and vigorous aerobic exercises.

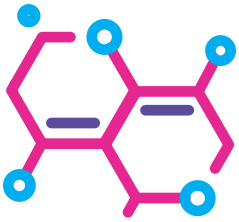
LIMIT YOUR INTAKE.
NOT DRINKING ALCOHOL IS BETTER FOR CANCER PREVENTION

There is no doubt that drinking alcohol can cause at least seven types of cancer, among them breast cancer. There are several reasons why drinking alcohol causes cancer. It is likely that different cancers are caused in different ways; alcohol (ethanol) is converted in our bodies into a chemical called acetaldehyde. Both ethanol and acetaldehyde are cancer-causing substances. Besides, alcohol can increase the levels of some hormones, such as oestrogen. High levels of oestrogen increase the risk of breast cancer. It is therefore important to restrict your alcohol intake to a minimal (less than 4 glasses of wine per week or equivalent).



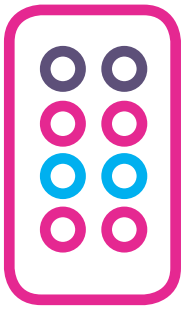
BREASTFEEDING REDUCES THE MOTHER'S CANCER RISK.

Women who breastfeed their babies for prolonged periods have a lower risk of developing breast cancer in later life than comparable women who do not breastfeed. The longer a woman breastfeeds, the more she is protected against breast cancer. The reduction in risk is about 4% for every cumulative 12 months of breastfeeding (i.e. obtained by summing up the periods a woman has breastfed each child), in addition to a reduction in breast cancer risk directly due to having had a baby.
The mechanism for the protective effect of breastfeeding is not fully understood. The beneficial effects may be explained by modifications of the structure of the breast and lower lifetime exposure to hormones in the mother.



HORMONE REPLACEMENT THERAPY (HRT) INCREASES THE RISK OF CERTAIN CANCERS.

Hormone replacement therapy is a specific type of hormonal drug usually prescribed for menopause symptoms in women.
Use of hormone replacement therapy increases the risk of breast cancer. The cancer risk pattern depends on the type of hormone replacement therapy (oestrogen-only or combined oestrogen-progestogen drugs), and whether the woman has had her uterus removed (undergone hysterectomy). Studies have shown that the excess risk of breast cancer associated with combined oestrogen-progestogen menopausal therapy occurs after a few years of treatment and remains elevated for at least five years after discontinuation of oestrogen-progestogen therapy, although the risk starts declining shortly after stop of treatment. Thus, the treatment should be taken for the shortest time and at the lowest dose possible to control the symptoms of menopause. Your individual risk-benefit ratio should be discussed with your referring physician or gynaecologist.



Note: Oral contraceptives, consisting of oestrogen and progestogen, possess both cancer-causing and cancer preventive properties. As oral contraceptives are used by healthy individuals any decision to use these drugs should be based on a thorough evaluation of the risk profile of the individual patient. Use of oral contraceptives is associated with a small excess risk of cancers of the breast, cervix, and liver; however, the use of these drugs also protects against endometrial and ovarian cancer. Therefore, from a cancer perspective, no clear recommendation can be given.

[31] Adapted from the European Code Against Cancer. International Agency for Research on Cancer. 2016.

ADDITIONAL RECOMMENDATIONS

Women with a germline genetic mutation will be advised for genetic counselling according to national guidelines and protocols.

For additional information on cancer prevention on different languages visit :

International Agency for Research on Cancer: https://cancer-code-europe.iarc.fr/index.php/en/

National Health Service – England: https://www.nhs.uk/conditions/breast-cancer/prevention/

Israel Cancer Association: http://www.cancer.org.il/template/default.aspx?pageid=6402

39. WHAT HAPPENS AT THE END OF THE STUDY?

At the end of the study, you will continue with standard follow-up/screening, regardless of the screening strategy to which you were allocated. You can discuss your continuing follow-up with your referring doctor* according to the standard of care at that time.

When results of the whole study are available, they will be communicated to you and all study participants and doctor-investigators as soon as possible.

Data obtained from study participants, including your data, may change future breast cancer screening in Europe. Once we publish the results of MyPeBS, and if personalised risk-based screening becomes the standard, you may be offered risk-based screening in the future.

The information concerning your continuing care, for up to 15 years after your entry into the study, is very important for us. However, the study follow-up only lasts for 4 years. We request that you give us permission to collect this longer-term information. If you agree, the confidential follow-up data at 15 years, after your entry into MyPeBS, will be transferred to us by your screening centre and/or for some countries the health insurance fund. An item on the last page of the informed consent form requests your permission for collecting this information. **You have the right to change your mind at any time without giving any justification. Your quality of care will not be affected in any way.**

40 IS FURTHER RESEARCH OR COMMERCIAL DEVELOPMENT BASED ON DATA FROM THIS STUDY FORESEEN?

The data collected during this study may be used for further research, such as research dedicated to better understanding of cancer risk or early detection or prevention of breast cancer. We will ask for your permission to use your pseudonymised* data for the purpose of further research.

This research may lead to commercial exploitation. For example, a new predictor of cancer risk may be commercialised. We will therefore also ask you at study entry whether or not you consent to the use of your pseudonymised* data for this purpose.

USING
MY PERSONAL SPACE
ON THE MyPeBS WEB PLATFORM

41. WHEN WILL I HAVE ACCESS TO MY PERSONAL DATA ON MyPeBS WEB PLATFORM?

Once you have joined the study, the doctor/ investigator (doctor or health care professional who will include you into the trial) will create your private access to the MyPeBS secured private web platform.

You will have access to your private space on the web platform through the MyPeBS public website (www.MyPeBS.eu), by using the username and password given to you by your doctor/investigator during visit 1.

42. WHICH PERSONAL INFORMATION WILL I FIND IN MY PERSONAL SPACE ON MyPeBS WEB PLATFORM?

On the web platform, you can access your personal space, your screening schedule, the questionnaires, study information, letters to print out for your various doctors, if necessary, and your risk profile if you were randomised in the personalised screening group, etc.

Your personal space on the web platform is private and confidential; all information is fully pseudonymised* outside this space.

43. IS IT NECESSARY FOR ME, AS A PARTICIPANT, TO HAVE ACCESS TO THE INTERNET THROUGHOUT THE STUDY?

Yes, you will need to have access to the internet throughout your study participation in order to check for information sent in the form of notifications to your email address, and to complete your follow-up data (once a year) and your psycho-social questionnaires (see question 44).

In addition, it is important to have the possibility to access to a mobile phone at the moment of the informed consent signature as you will receive a text containing your personal code, to be entered in the web platform to allow electronic signature (authentication step).

44. HOW CAN I UPDATE MY PERSONAL INFORMATION DURING THE PROJECT?

It is very important that you update your personal information at any time throughout your participation in the study by connecting to your private area on the web platform.

Please indicate any change to your personal or family medical history (e.g. breast radiological examinations you have undergone, breast biopsy you have had, cancer diagnosis in your family) or any new personal information you consider relevant (for example if you move to another region/country).

If you become pregnant during the study, please declare it in your personal space in the web platform and inform your study doctor /investigator immediately, so that your screening schedule can be revised accordingly.

You will receive a yearly reminder asking you to update your data (if needed).

If you have been randomised to the "risk-based screening" group your estimated individual breast cancer risk may change over time, depending on changes in personal characteristics and family history. For this reason it is very important that you continually update the information in the secure study web platform. Your personal risk will be reassessed and updated. If your risk category/level changes after a significant event (such as a new case of breast cancer in your family or if you have had a breast biopsy etc.), a new breast screening schedule (mammography with or without ultrasound or MRI) will be sent to you. Your next visit will follow this new screening schedule. If you have any questions, please do not hesitate to discuss these with your study doctor / investigator.

45. WHAT HAPPENS IF I EXPERIENCE A TECHNICAL PROBLEM (E.G. I CANNOT ENTER INTO MY PRIVATE SPACE ON MyPeBS WEB PLATFORM OR I HAVE LOST MY USERNAME OR PASSWORD)?

If you forgot/lost your password, please click on "forgotten password" on the web platform connexion page, and you will be sent an email that will allow you to choose a new one.

If you forgot/lost your username, please refer to the very first e-mail that was sent to you, that contained the details to connect to your personal space in the web platform: it is the number indicated after "login".

You can also find this number on the imaging exam calendar that was given to you: it is the number indicated after "study code". If you still cannot find it, please contact doctor/investigator who will be able to provide it to you.

In case of technical problem, please contact doctor/investigator, who will then contact the study sponsor.

SAFETY, ETHICS AND TREATMENT

46. WHO IS RESPONSIBLE FOR STUDY CONDUCT AND DATA MANAGEMENT?

Unicancer is the sponsor of this study and is responsible for study conduct and data management. In addition, the study is supervised and controlled by the executive committee of MyPeBS project and by the MyPeBS clinical study steering committee, which can be advised by an independent ethics & data monitoring committee.

47. WHO IS RESPONSIBLE FOR ENSURING THAT WOMEN'S SAFETY AND RIGHTS ARE PROTECTED IN MyPeBS?

The sponsor (Unicancer) has taken all the necessary measures required by the law to protect all the women who participate in this study. The study will be conducted in compliance with the current Declaration of Helsinki, the current ICH Harmonised Tripartite Guideline for Good Clinical Practice (ICH-GCP), the European Directive 2001/20/CE on the conduct of clinical studies and subsequent texts (Eudralex Vol 10), the European regulation on data protection (EU) 2016/679 (General Data Protection Regulation) and each respective national legal requirement where applicable.

Unicancer shall assume liability for any injuries sustained by any person participating in the interventional research, and has taken out an interventional research insurance in accordance with current legislation. This insurance certificate can be consulted at your investigational centre upon request.

Where the sponsor's liability is not engaged, the participants may claim compensation according to country specificities.

48. WHICH AUTHORITIES HAVE ASSESSED THE SCIENTIFIC RELEVANCE AND CONDITIONS GOVERNING PARTICIPANT'S PROTECTION AND THE TRIAL'S COMPLIANCE WITH THEIR RIGHTS?

The terms and conditions of the MyPeBS study protocol have been submitted for all required authorisations in each country, whether competent for scientific and statistical aspects or for ethical or data protection aspects of clinical research.

49. IS PARTICIPATING IN MyPeBS MANDATORY?

No, your participation in this study is of course on a voluntary basis.

50. IF I REFUSE TO PARTICIPATE IN MyPeBS, WILL IT AFFECT MY PARTICIPATION IN THE STANDARD BREAST CANCER SCREENING PROGRAM IN ANY WAY?

Absolutely not. Whether you agree to participate or not will not affect your participation in the standard breast cancer screening programme currently ongoing in your country. In other words, if you do not want to participate in the study, nothing will happen and you will continue to be invited to the standard breast cancer screening programme in your country.

51. CAN I STOP PARTICIPATING IN MyPeBS AND WOULD IT HAVE CONSEQUENCES FOR MY CURRENT AND FUTURE CARE?

Once you have accepted to participate in the MyPeBS study, you can decide to stop at any time. You have the right to change your mind at any time without giving any justification; this would have absolutely no consequence on the care you receive.

If you decide to leave the study early, you only need to inform your study doctor / investigator.

Similarly, the study doctor/investigator may decide to withdraw you from the study if she/he believes it is in your best interest.

52. WILL MY GENERAL PRACTITIONER BE AUTOMATICALLY INFORMED OF MY PARTICIPATION IN MyPeBS?

Depending on your country of residence, your general practitioner may not be informed automatically of your participation in the study.

Please use the standard letters available in your private space of the web platform to inform all health care professionals you think useful of your participation.

53. ARE MY PERSONAL INFORMATION DATA PROTECTED?

All your personal data will be pseudonymised* so that it will be absolutely impossible to identify you outside of your personal secured space in the participants' portal of the study.

Your personal medical records, which are subject to professional secrecy, will remain **confidential** and can only be consulted under the supervision of your study doctor /investigator, or upon request of a Health Authority.

The processing of your data is necessary for the realisation of the scientific research in accordance with the legitimate objectives of UNICANCER and conducted in the public interest in the field of public health (article 6.1.e, and 9.2.j of Regulation (EU) No. 2016/679). Consequently, as stated above, pseudonymised* data needed to answer the scientific questions of this research conducted in the interest of public health, will be collected, sent and processed by Unicancer, the sponsor, and its services providers in the strict framework of the

achievement of their missions. These data will be treated confidentially to allow analysis of the research results.

If you agree, the pseudonymised* data collected during the trial may be used by Unicancer or its duly authorised partners in the MyPeBS project in a confidential and secure manner in order to continue breast cancer screening research.

Your data will be kept for up to two years after the last scientific publication related to research projects. They will then be archived, with very limited access, for a maximum duration of twenty-five years.

You have the following rights on the data concerning you, according to the conditions provided for by the regulations in force:

- a right of access to your personal data,
- a right to rectification of inaccurate personal data,
- a right to request the erasure of your personal data,
- a right to restrict the processing of your personal data particularly if the processing is called into question.

You have also the right to object to the processing of your personal data. This prevents, in particular, further data collection by the data controller.

If you exercise your right of objection or erasure, the data controller may store and analyse data that has already been collected in so far as its deletion is likely to render impossible or seriously impair the achievement of the objectives of the processing, or if there is a compelling legitimate reason for processing the data, such as ensuring the reliability of the research results, responding to a request from the public authorities, or in order to comply with a legal obligation which requires processing by Union or Member State law to which the controller is subject or for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller.

These rights are exercised by the Data protection Officer of the study sponsor (UNICANCER): Data Protection officer, 101 rue de Tolbiac 75654 Paris Cedex 13 – dpo@unicancer.fr.

If, despite UNICANCER's undertaking to protect your rights and your personal data, you are not satisfied with the protection of your data, you have the right to file a complaint with your respective national control authority.

54. WHAT ARE MY RIGHTS RELATED TO BIOLOGICAL SAMPLES?

In accordance with current bioethics laws, the use of your saliva for genetic testing as part of the present study (evaluation of breast cancer risk specific genetic polymorphisms*) is subject to your prior, written consent.

Additionally, if you give your approval for further research on your biological samples (see consent sheet), your saliva sample residue will be stored in a centre (located in France) ensuring their protection and their confidentiality. This will be done in accordance with applicable legislation, for future research particularly in the fileds of cancer, prevention, or nutrition and genetics, as long as the samples remain of scientific interest. You can however object to this if you wish so, by asking your study doctor / investigator. You may also, at any time during the research, ask your study doctor / investigator to destroy the samples. Part of the biological material may be transferred as part of research collaborations to other institutions or private companies, in accordance with the applicable Bioethics Law.

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55. WILL I RECEIVE INFORMATION ON THE STUDY RESULTS?

According to the applicable law (2002-2003 dated 4 March 2002) relative to patient's rights, you will be informed of the overall study results upon request made to any of the doctors who were involved in your screening schedule during the study. The overall study results will also be made available on the MyPeBS public website upon study termination and publication.

GLOSSARY

Breast density: The relative proportion of dense to fatty tissue in the breast on a mammogram. The higher the density, the harder it may be to find abnormalities in a mammogram, and the higher the individual risk of developing breast cancer.

Breast MRI examination: Magnetic resonance imaging (MRI) is an examination used to record two or three-dimensional views of the breast. The MRI-scan provides information on lesions that cannot be seen by standard X-rays, or ultrasound.

Breast ultrasound: Procedure performed by a radiologist using ultrasound, in order to study the internal breast tissue. It is a painless procedure.

Digital breast tomosynthesis (DBT): This new technology produces 3 dimensions (3D) and reconstructed (synthetic) 2D images of the breast. It has been recommended by the European Guidelines as an option instead of standard mammography.

DNA: Deoxyribonucleic acid, is a biological macromolecule found in all cells of the human body. DNA contains genetic information in the form of tens of thousands of genes coding for proteins that enable the development, function, and reproduction of human beings.

False positive: Mammograms that lead to check-ups or a biopsy when in fact the lesion is completely benign/non-cancerous.

Genetic polymorphisms: Normal but rare variants in gene sequences potentially related to a different function of the protein coded by the gene. Polymorphisms enable genetic variety but can also be associated with different levels of sensitivity to certain substances or drugs, or a different risk of certain diseases.

Interval cancers: Breast cancers appearing between two negative screening episodes.

Interventional research: Research on humans including an intervention on the person (i.e., a diagnostic procedure, treatment, or monitoring). The care strategies, and diagnostic and monitoring procedures are determined in advance by a research protocol.
Invasive: term describing cancer able to invade surrounding tissue and to potentially metastase.

Mammogram: Radiological examination of the breasts with two images per breast.

Overdiagnosis: Approximately 1 in 10 of the breast cancers detected by screening are growing so slowly that they would never cause problems during the woman's life. These cases are called "overdiagnoses" and they lead to unnecessary anticancer treatments (called **overtreatments**).

Overtreatment: See above.

Pre-cancerous lesions: Is a term to use to describe certain conditions or lesions involving abnormal cell which are associated with an increased risk of developing into cancer.

Predisposition: Set of factors, in an individual, which increase the risk of developing a specific disease.

Pseudonymisation: The replacement of all data (in a database etc.) that identifies a person with an artificial identifier.

Radio-induced breast cancer: Cancer caused by long-term exposure to small doses of X-rays.

Randomisation: Random allocation/assignment, by a computer, to randomly divide people participating in the study between two (or more) groups.

Referring doctor: Doctor looking after you day by day (in general, it is your general practitioner).

Stage 2 and higher breast cancer: Breast tumour 2 cm or larger or with the cancer having spread to the axillary lymph node.

Study doctor/nvestigator: A health professional directing and monitoring a clinical trial and ensuring management of the patients participating in that trial.

Ultrasound: Breast examination with sound waves to create medical images of the breast tissue.